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Spread of community-acquired meticillin-resistant *Staphylococcus aureus* skin and soft tissue infection within a family: implications for antibiotic therapy and prevention.

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Summary

Outbreaks or clusters of community-acquired meticillin-resistant *Staphylococcus aureus* (CA-MRSA) within families have been reported. We describe a family cluster of CA-MRSA skin and soft-tissue infection where CA-MRSA was suspected because of recurrent infections which failed to respond to flucloxacillin. While the prevalence of CA-MRSA is low worldwide, CA-MRSA should be considered in certain circumstances depending on clinical presentation and risk assessment. Surveillance cultures of family contacts of patients with MRSA should be considered to help establish the prevalence of CA-MRSA and to inform the optimal choice of empiric antibiotic treatment.

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1 **Introduction**

2 Meticillin-resistant *Staphylococcus aureus* (MRSA) has been traditionally associated with
3 healthcare-associated (HA) infections. Established risk factors for HA-MRSA infections
4 include recent hospitalization or surgery, dialysis, residence in a long-term care facility, and
5 indwelling catheters or percutaneous medical devices (Naimi *et al.*, 2003). However, new
6 strains of MRSA have emerged in the community which cause infection in patients who have
7 no previous history of direct or indirect healthcare contact. These infections are referred to as
8 community-acquired or community-associated MRSA (CA-MRSA). The isolates causing
9 these infections are reported to be genetically and phenotypically distinct from HA-MRSA as
10 the strains are typically more susceptible to a wider range of anti-staphylococcal antibiotics
11 and often produce the Panton-Valentine leukocidin (PVL) toxin (Vandenesch *et al.*, 2003).

12
13 CA-MRSA infections have been reported in North America, Europe, Australia and New
14 Zealand (Vandenesch *et al.*, 2003; Dufour *et al.*, 2002; Okuma *et al.*, 2002; Adhikari *et al.*,
15 2002). Most cases have been associated with skin and soft tissue infection (SSTI) or
16 necrotising pneumonia. Here, we described intra-familial spread of CA-MRSA associated
17 with SSTI and discuss its implications.

Case Report

A previously healthy 42-year-old mother presented to her general practitioner with an abscess on her leg. She gave a history of two previous abscesses on her legs and buttock in the last seven months. She received several courses of oral flucloxacillin with some clinical resolution of the abscess on each occasion and no specimen was sent for culture. A few days prior to the most recent presentation, her husband presented with an abscess on his face and 14 days later, their 5-year-old son presented with a boil on his nose. Neither her husband nor her son presented with previous history of soft tissue infection.

Swabs were taken from the abscesses and the boil. MRSA were isolated from the swabs from these three family members. Both parents were treated with oral doxycycline with no further recurrence of their abscesses; the son did not require systemic antibiotics. Two other sons were MRSA-negative on screening. On further enquiry, the family reported no involvement with contact sports, animal contacts or contact with known MRSA carriers. Both parents are from the European Union, with the mother having been born and educated in Ireland. There was no migration background and no travel history in the last two years such as to Australia and New Zealand. Consequently, the original source of these isolates remains unknown.

Isolate identification and antimicrobial susceptibility testing was performed initially using an automated system (PhoenixTM 100: BD Biosciences, Sparks, MD, USA). Susceptibility was confirmed by disk diffusion according to Clinical and Laboratory Standards Institute methodology (CLSI, 2007). All three isolates were resistant to β -lactam antibiotics and susceptible to aminoglycosides, chloramphenicol, ciprofloxacin, erythromycin, fusidic acid,

lincomycin, linezolid, mupirocin, rifampicin, tetracycline, trimethoprim and vancomycin. The isolates were also susceptible to daptomycin with E-test minimum inhibitory concentration (MIC) of <1 mg/L and to tigecycline with MIC of 0.5 mg/L; the breakpoint for daptomycin according to CLSI 2009 guidelines and for tigecycline by Kronval *et al* 2006. Further characterisation showed the isolates to be urease-positive and to carry the genes encoding the PVL toxin. DNA macro-restriction analysis yielded a pattern designated 02033 which is indistinguishable from the pattern exhibited by CA-MRSA isolates reported from Ireland that belonged to multilocus sequence type (MLST) ST30 and carried the staphylococcal cassette chromosome *mec* (SCC*mec*) type IV element (Rossney *et al.*, 2007). Staphylococcal protein A (*spa*) gene sequence typing showed that the isolates belonged to *spa* type t019. This *spa* type is also associated with ST30 according to data held in the Ridom Spa Server database (<http://spaserver.ridom.de>).

Discussion

The overall prevalence of CA-MRSA is low worldwide but there is evidence that this is increasing mainly in the USA, Canada, Australia, Greece and Denmark (Salgado *et al.*, 2003; Vourli *et al.*, 2009; Sdougkos *et al.*, 2008; Larsen *et al.*, 2009). CA-MRSA is also an emerging challenge in Ireland (Rossney *et al.*, 2007). Clusters and outbreaks of CA-MRSA have been described in specific groups of individuals such as Native Americans in the USA, men who have sex with men, prison inmates, military recruits, competitive sports participants and children attending childcare centres (Weber, 2005). Several risk factors for CA-MRSA acquisition have been identified. These include crowded living conditions, closed communities with people in close contact, participation in contact sports, poor hygiene, compromised skin integrity, exposure to contaminated items, prior MRSA infection and

1 previous antibiotic exposure (HPA, 2008; Popovich & Hota, 2008). None of these risk factors
2 applied to the family cluster reported here.

3
4 The spectrum of clinical infections caused by CA-MRSA differs from that caused by HA-
5 MRSA. HA-MRSA isolates commonly cause bloodstream, urinary tract and respiratory tract
6 infections. CA-MRSA infections are more likely to involve SSTI (Naimi *et al.*, 2003).
7 However, severe necrotising pneumonia due to CA-MRSA has occasionally been described
8 (Jones *et al.*, 2006; Gorak *et al.*, 1999). The case described in the present report is intra-
9 familial spread of CA-MRSA infection in a family cluster characterised by SSTI with no
10 history of risk factors for HA-MRSA.

11
12 The optimal management of *S. aureus* SSTI with abscesses formation especially abscesses
13 less than 5 cm in diameter is incision and drainage without adjunctive antibiotics. However,
14 systemic antibiotics should be considered in immunocompromised patients, infants, patients
15 with multiple areas of skin and soft tissue infections (especially abscesses >5cm), infections
16 that do not respond to incision and drainage or if there is clinical deterioration (HPA, 2008;
17 Popovich & Hota, 2008). Compared with MRSA, meticillin-susceptible *S. aureus* (MSSA) is
18 still the more prevalent cause of SSTI in the community and a recent study has shown that
19 62% of PVL-positive *S. aureus* isolates (444/720) were MSSA (HPA, 2008). Therefore β -
20 lactam antibiotics are still the choice for empiric therapy for the young and for clinically
21 stable patients in the community. However, CA-MRSA should be suspected if there are
22 recurrent skin infections or abscesses that are unresponsive to β -lactam therapy and/or if there
23 is a history of spread within the family. Specimens for culture should be taken in the

community by general practitioners if the infection persists or progresses while the patient is receiving appropriate antibiotics directed towards MSSA.

Meticillin resistance in *S. aureus* is mediated by the *mecA* gene which encodes an altered penicillin binding protein (PBP) PBP2a with low affinity for β -lactam antibiotics. The *mecA* gene together with its regulators, *mecI* and *mecR* is carried on the SCC*mec* mobile element. There are at least seven main types of SCC*mec* (types I–VII) and numerous subtypes SCC*mec* (Deurenberg &, Stobberingh 2009). CA-MRSA is associated with the SCC*mec* elements SCC*mec* types IV and V (Rossney *et al.*, 2007; Vourli *et al.*, 2009; Sdougkos *et al.*, 2008; Larsen *et al.*, 2009; Otter *et al.*, 2009). CA-MRSA frequently carries the *pvl* genes which code for a cytotoxin that causes tissue necrosis and leucocyte destruction by forming pores in cellular membrane. PVL is an established virulence factor in the pathogenesis of infection associated with CA-MRSA but other factors such as the arginine catabolism mobile element (ACME), and/or other cytolytic peptides may also be important (Diep *et al.* 2008; Tseng *et al.* 2009; HPA, 2008; Labandeira-Rey *et al.*, 2007; Gillet *et al.*, 2002).

It is reported that CA-MRSA strains can be distinguished from HA-MRSA strains because they are generally susceptible to antimicrobials other than β -lactams and carry the *pvl* genes (Naimi *et al.*, 2003). It is also reported that CA-MRSA from different geographic areas exhibit different MLSTs with ST80 being associated with Europe, ST93 with Australia, ST30 with Oceania, and ST1, ST59 and ST8 with the USA (Vandenesch *et al.*, 2003). A recent study showed that PVL-positive CA-MRSA from Ireland exhibited a range of six MLST types with ST30 and ST8 occurring most frequently and that only 6.7% of CA-MRSA carried the *pvl* genes (Rossney *et al.*, 2007). In that study, 36% of *pvl*-positive isolates came from

1 patients of non-Irish ethnic origin. An earlier study from Ireland had also shown that the
2 predominant strain among HA-MRSA exhibited a non-multi-antibiotic-resistant phenotype
3 and carried SCCmec IV (Rossney *et al.*, 2006). Hence neither carriage of *pvl* genes or
4 SCCmec IV nor a susceptible antibiogram can be used as sole markers for CA-MRSA in
5 Ireland (Rossney *et al.*, 2007) and a time-based definition such as detection of MRSA within
6 24 or 48 hours of hospital admission or detection in a patient without healthcare-associated
7 risk factors must be used.

8
9 Screening and decolonisation therapy are important components in the prevention and control
10 of HA-MRSA (Kluytmans *et al.*, 1997; Davis *et al.*, 2004; Cosgrove *et al.*, 2003). Studies
11 have shown that the identification of CA-MRSA colonisation may require screening of sites
12 other than the nares but the efficacy of CA-MRSA decolonisation is unclear (Popovich &
13 Hota, 2008; Zafar *et al.*, 2007). Guidelines for the management of PVL-associated *S. aureus*
14 in England recommend topical decolonisation without prior screening of the primary case
15 (HPA, 2008). Decolonisation therapy is also part of the MRSA control guidelines in
16 Denmark and Greece (Vourli *et al.*, 2009; Larsen *et al.*, 2009). Screening and decolonisation
17 of contacts should be considered where close contacts are infected or where they pose a
18 special risk to others (e.g. healthcare workers). However, the key principles of prevention and
19 control of CA-MRSA are early diagnosis and treatment, ensuring lesions are covered with
20 clean dressings, good personal hygiene, not sharing personal items, laundry using a hot-wash
21 cycle, regular household cleaning and the avoidance of communal and recreational settings
22 by infected patients. Patients in occupations at high risk for transmission of CA-MRSA such
23 as healthcare workers should be excluded from work until lesions have healed (HPA, 2008).

- 1 Surveillance for CA-MRSA is important as information is needed on the baseline frequency
- 2 of CA-MRSA colonisation in Ireland compared with other countries. Increasing CA-MRSA
- 3 prevalence will affect the choice of appropriate empiric antibiotics to optimise patient care
- 4 and may pose risk of hospital spread if infected patients require admission to hospital.

REFERENCES

- Adhikari, R. P., Cook, G. M., Lamont, I., Lang, S., Heffernan, H., Smith, J. M. (2002).** Phenotypic and molecular characterization of community occurring, Western Samoan phage pattern methicillin-resistant *Staphylococcus aureus*. *J Antimicrob Chemother* **50**, 825-831.
- CLSI, (2009).** Performance Standards for Antimicrobial Susceptibility Testing; Sixteenth Informational Supplement. CLSI Document M100-S16. Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
- CLSI, (2007).** Performance Standards for Antimicrobial Susceptibility Testing; Sixteenth Informational Supplement. CLSI Document M100-S16. Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
- Cosgrove, S. E., Sakoulas, G., Perencevich, E. N., Schwaber, M. J., Karchmer, A. W. & Carmeli, Y. (2003).** Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteraemia: a meta-analysis. *Clin Infect Dis* **36**, 53-59.
- Davis, K. A., Stewart, J. J., Crouch, H. K., Florez, C. E. & Hospenthal, D. R.(2004).** Methicillin-resistant *Staphylococcus aureus* (MRSA) nares colonisation at hospital admission and its effect on subsequent MRSA infection. *Clin Infect Dis* **39**, 776-782.
- Deurenberg, R.H. & Stobberingh E.E.(2009).** The molecular evolution of hospital- and community-associated methicillin-resistant *Staphylococcus aureus*. *Curr Mol Med* **9**(2), 100-115.
- Diep, B.A., Palazzolo-Ballance, A.M., Tattevin, P., Basuino, L., Braughton, K.R., Whitney, A.R., Chen, L., Kreiswirth, B.N., Otto, M., DeLeo, F.R., Chambers, H.F. (2008).** Contribution of Panton-Valentine leukocidin in community-associated methicillin-resistant *Staphylococcus aureus* pathogenesis. *PLoS One* **12**; 3(9), e3198.
- Dufour, P., Gillet, Y., Bes, M., Lina, G., Vandenesch, F., Floret, D., Etienne, J. & Richet, H. (2002).** Community-acquired methicillin-resistant *Staphylococcus aureus* infection in France: emergence of a single clone that produces Panton-Valentine leukocidin. *Clin Infect Dis* **35**, 819-824.
- Gillet, Y., Issartel, B., Vanhems, P., Fournet, J. C., Lina, G., Bes, M., Vandenesch, F., Piémont, Y., Brousse, N., Floret, D., Etienne, J. (2002).** Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients. *Lancet* **359**, 753-759.

1 **Gorak, E. J., Yamada, S. M. & Brown, J. D. (1999).** Community-acquired methicillin-
2 resistant *Staphylococcus aureus* in hospitalized adults and children without known risk
3 factors. *Clin Infect Dis* **29**, 797-800.

4 **HPA (2008).** Guidance on the diagnosis and management of PVL-associated
5 *Staphylococcus aureus* infections (PVL-SA) in England. Report prepared by the PVL
6 sub-group of the Steering Group on Healthcare Associated Infection.
7 http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1218699411960.

8 **Jones, T. F., Creech, C. B., Erwin, P. Baird, S. G., Woron, A. M. & Schaffner, W.**
9 **(2006).** Family outbreaks of invasive community-associated methicillin-resistant
10 *Staphylococcus aureus* infection. *Clin Infect Dis* **42**, e76-78.

11 **Kluytmans, J., van Belkum, A. & Verbrugh, H. (1997).** Nasal carriage of
12 *Staphylococcus aureus* epidemiology, underlying mechanisms, and associated risks. *Clin*
13 *Microbiol Rev.* **10**, 505-520.

14 **Kronvall, G., Karlsson, I., Walder, M., Sörberg, M. & Nilsson, L.E. (2006).**
15 Epidemiological MIC cut-off values for tigecycline calculated from Etest MIC values
16 using normalized resistance interpretation. *J Antimicrob Chemother* **57**(3), 498-505

17 **Labandeira-Rey, M., Couzon, F., Boisset, S., Brown, E. L., Bes, M., Benito, Y.,**
18 **Barbu, E. M., Vazquez, V., Höök, M. & other authors (2007).** *Staphylococcus aureus*
19 Panton-Valentine leukocidin causes necrotizing pneumonia. *Science* **315**, 1130-1133.

20 **Larsen, A. R., Stegger, M., Bocher, S., Sorum, M., Monnet, D. L. & Skov, R. L.**
21 **(2009).** Emergence and characterization of community-associated methicillin-resistant
22 *Staphylococcus aureus* infections in Denmark 1999-2006. *J Clin Microbiol* **47**, 73-78.

23 **Naimi, T. S., Ledell, K. H., Como-Sabetti K, Borchardt, S. M, Boxrud, D. J.,**
24 **Etienne, J., Johnson, S. K., Vandenesch, F., Fridkin, S., O'Boyle, C., Danila, R. N. &**
25 **Lynfield, R. (2003).** Comparison of community- and healthcare- associated methicillin-
26 resistant *Staphylococcus aureus* infection. *JAMA* **290**, 2976-2984.

27 **Okuma, K., Iwakawa, K., Turnidge, J. D., Grubb, W. B., Bell, J. M., O'Brien, F. G.**
28 **Coombs, G. W., Pearman, J. W., Tenover, F. C. & other authors (2002).**
29 Dissemination of new methicillin-resistant *Staphylococcus aureus* clones in the
30 community. *J Clin Microbiol* **40**, 4289-4294.

31 **Otter, J. A., Havill, N. L., Boyce, J. M. & French, G. L. (2009).** Comparison of
32 community-associated methicillin-resistant *Staphylococcus aureus* from teaching
33 hospitals in London and the USA, 2004-2006: where is USA300 in the UK? *Eur J Clin*
34 *Microbiol Infect Dis* **28**, 835-839

35 **Popovich, K. J. & Hota, B. (2008).** Treatment and prevention of community-associated
36 methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections. *Dermatol Ther*
37 **21**, 167-179.

38 **Rossney, A. S., Lawrence M. J., Morgan, P. M., Fitzgibbon, M. M., Shore, A.,**
39 **Coleman, D. C., Keane, C. T. & O'Connell, B. (2006).** Epidemiological typing of
40 MRSA isolates from blood cultures taken in Irish hospitals participating in the European

- Antimicrobial Resistance Surveillance System (1999-2003). *Eur. J. Clin. Microbiol. Infect. Dis* **25**, 79-89.
- Rossney, A. S., Shore, A. C., Morgan, P. M., Fitzgibbon, M. M., O'Connell, B. & Coleman D. C. (2007).** The emergence and importation of diverse genotypes of methicillin-resistant *Staphylococcus aureus* (MRSA) harbouring the Panton-Valentine leukocidin gene (*pvl*) reveal that *pvl* is a poor marker for community-associated MRSA strains in Ireland. *J Clin Microbiol* **45**, 2554-2563.
- Salgado, C. D., Farr, B. M. & Calfee, D. P. (2003).** Community-acquired methicillin-resistant *Staphylococcus aureus*: a meta-analysis of prevalence and risk factors. *Clin Infect Dis* **36**, 131-139
- Sdougkos, G., Chini, V., Papanastasiou, D. A., Christodoulou, G., Stamatakis, E., Vris, A., Christodoulidi, I., Protopapadakis, G. & Spiliopoulouet, I. (2008).** Community-associated *Staphylococcus aureus* infections and nasal carriage among children: molecular microbial data and clinical characteristics. *Clin Microbiol Infect* **14**, 995-1001.
- Tseng, C.W., Kyme, P., Low, J., Rocha, M.A., Alsabeh, R., Miller, L.G., Otto, M., Arditi, M., Diep, B.A., Nizet, V., Doherty, T.M., Beenhouwer, D.O., Liu, G.Y. (2009).** *Staphylococcus aureus* Panton-Valentine leukocidin contributes to inflammation and muscle tissue injury. *PLoS One* **27**; 4(7), e6387.
- Vandenesch, F., Naimi, T., Enright, M. C., Lina, G., Nimmo, G. R., Heffernan, H., Liassine, N., Bes, M., Greenland, T., Marie-Elisabeth Reverdy, M. E. & Etienne, J. (2003).** Community-acquired methicillin-resistant *Staphylococcus aureus* carrying Panton-Valentine leukocidin genes: worldwide emergence. *Emerg Infect Dis* **9**, 978-984.
- Vourli, S., Vagiakou, H., Ganteris, G., Orfanidou, M., Polemis, M., Vatopoulos, A., & Malamou-Ladas, H. (2009).** High rates of community-acquired, Panton-Valentine leukocidin (PVL)-positive methicillin-resistant *S. aureus* (MRSA) infections in adult outpatients in Greece. *Euro Surveill* **14**(2).
- Weber, J. T. (2005).** Community-associated methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* **41**, S269-272.
- Zafar, U., Johnson, L. B., Hanna, M., Riederer, K., Sharma, M., Fakih, M. G., Thirumoorthi, M. C., Farjo, R. & Khatib, R.(2007).** Prevalence of nasal colonization among patients with community-associated methicillin-resistant *Staphylococcus aureus* infection and their household contacts. *Infect Control Hosp Epidemiol* **28**, 966-999,